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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,856	01/07/2002	Susan Slaugenhaupt	1829-4004US1	5418

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EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/041,856	SLAUGENHAUPT ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50,61, 65-68 and 76-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *61 and 68* is/are allowed.

6)☒ Claim(s) *50,65-67 and 76-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: sequence alignment of SEQ ID NO: 2 and AR070165 (Cohen et al US Patent No. 5891719).

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 2, 2006 has been entered.

Applicant's amendments and arguments set forth in the response of June 2, 2006 have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. The following Office action contains new and modified grounds of rejection and is made non-final.

Claims 50, 61, and 65-80 are pending and have been examined herein.

2. It is noted that claims 61 and 65 refer to an IKAP gene, whereas claims 66 and 67, which depend from claim 61 refer to the IKBKAP gene. The claims should consistently refer to the gene by the same acronym and should preferably refer only the IKBKAP gene, as supported by the specification.

Priority

3. A claim as a whole is assigned an effective filing date (rather than the subject matter within a claim being assigned individual effective filing dates). Claims 50 and 76 encompass the full length sequence of SEQ ID NO: 1. These claims are not entitled to priority to provisional application 60/260,080. Provisional

application 60/260,080 provides a transmission letter stating that 56 sheets of drawings were filed. However, this application was not filed with a complete set of drawings. While Figure 6 states that the recited sequence is of a length of 66476 nucleotides, the drawing ends at nucleotide 53,050. Accordingly, the provisional application does not provide support for the presently claimed nucleic acids of SEQ ID NO: 1 (having a length of 66,476 nucleotides. Thereby, these claims are not entitled to the priority of the provisional application and are entitled to the filing date of January 7, 2002.

Claims 78 and 80 are not entitled to the filing date of the '080 application because the '080 application does not disclose the nucleotide sequence of SEQ ID NO: 2. The response of June 2, 2006 states that the '080 application "states" the sequence of GenBank Accession No. AF153419. However, the '080 application recites only a reference to GenBank Accession No. AF153419. The application did not disclose/recite the specific sequence of GenBank Accession No. AF153419. Also, the '080 application did not specifically incorporate by reference the sequence of GenBank Accession No. AF153419. As stated in MPEP 608.01(p)[R-2] "While the prior art setting may be mentioned in general terms, the essential novelty, the essence of the invention, must be described in such details, including proportions and techniques, where necessary, as to enable those persons skilled in the art to make and utilize the invention. A reference to a GenBank Accession Number constitutes an improper incorporation by reference to essential subject matter since this subject matter is

necessary to describe the claimed invention. Essential material may not be incorporated by reference to non-patent publications (see MPEP 608.01(p)). Further, there is no evidence of record to establish that the presently claimed SEQ ID NO: 2 is identical to the sequence of GenBank Accession NO. AF153419 as it appeared as of the filing date of the '080 application. In fact, the sequence does not appear to be identical to that of present SEQ ID NO: 2 since the response of June 2, 2006 states that "(s)ubsequent to filing of the provisional application, the sequence submitted under Accession No. AF153419 was revised at the non-coding 3' end." The response further asserts that the 3' coding region is not relevant to the presently claimed invention since the portion of the sequence that is to be used in the context of the invention has not been changed. However, a claim as a whole is entitled to a filing date and not the individual elements of a claim. In the present situation, priority must be provided to the complete sequence of SEQ ID NO: 2 and not just to the "relevant" portions of SEQ ID NO: 2.

Additionally, claims 77 and 79 are not entitled to the filing date of provisional application '080 because this application does not appear to provide support for the concept of nucleic acids consisting of nucleotides 16 nucleotides selected from the specific region of exon 19 to exon 20 of SEQ ID NO: 1 (see below). Claim 65 does not appear to be entitled to the filing date of the '080 application because this application does not appear to disclose a kit wherein the primers of SEQ ID NO: 19 and 23 are used to amplify a region of sufficient size to detect both the FD1 and FD2 mutations (see below). Also, claims 66 and 67

are not entitled to the filing date of the '080 application because the '080 application does not appear to specifically disclose kits which amplify "a region extending from the beginning of exon 18 through exon 23 of SEQ ID NO: 1" (claim 66) or "a region extending from the beginning of exon 19 through exon 23 of SEQ ID NO: 1" (claim 67).

The following are new grounds of rejection:

Claim Rejections - 35 USC § 112

4. Claims 65-67, 77 and 79 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as originally filed does not appear to provide support for the recitation in claim 65 of a kit comprising the primers of SEQ ID NO: 83 and 84 which are "capable of amplifying a region of IKBKAP of sufficient size to detect a FD1 or FD2 mutation, wherein said region amplified comprises a FD1 or FD2 mutation." The FD1 mutation occurs at bp 6 of intron 20, and the FD2 mutation occurs at bp 73 of exon 19 (page 3 of the specification). The specification does not disclose the location of the intron/exon boundaries of the IKBKAP gene, nor the location within the IKBKAP gene to which the primer of SEQ ID NO: 19 and 23 hybridize. However, it appears that the primer of SEQ ID NO: 83 hybridizes to nucleotide positions 33,713 to 33,731. While this region overlaps the mutation at position 33,714 (i.e., this position is 2 nucleotides from

the 5' terminus of the primer), the specification does not specifically disclose the use of the primer pair of SEQ ID NO: 19 and 23 to detect the FD2 mutation. In particular, there is no disclosure as to a method in which the primer containing a G at the mutated position is used to detect a C at the mutated position. Thereby, it does not appear that the specification as originally filed provides support for a kit containing the set of primers of SEQ ID NO: 19 and 23, wherein the primers amplify a region containing both the FD1 and FD2 mutations and wherein the primers can be used to detect both the FD1 and FD2 mutation.

Regarding claims 66 and 67, the specification as originally filed does not appear to provide support for the recitations of "a region extending from the beginning of exon 18 through exon 23 of SEQ I D NO: 1" (claim 66) or "a region extending from the beginning of exon 19 through exon 23 of SEQ ID NO: 1" (claim 67). The response of June 2, 2006 points to Figure 1 as providing support for this embodiment. However, while Figure 1 shows that the primer of SEQ ID NO: 84 hybridizes to exon 18, the primer of SEQ ID NO: 83 hybridizes to exon 19 and the primer of SEQ ID NO: 84 hybridizes to exon 23, Figure 1 does not disclose the specific location to which these primers hybridize within exons 18, 19 and 23. Again, the specification does not disclose the nucleotide positions of the intron/exon boundaries of the IKBKAP gene. The response of June 2, 2006 does state that exon 19 through 20 corresponds to nucleotides 33,642 to 34,195 of SEQ ID NO: 1. However, no documentation or other evidence has been provided to support this conclusion. If this statement is correct, then the primer of

SEQ ID NO: 19 does not appear to amplify the beginning of exon 19 since this primer hybridizes to nucleotides 33,713 to 33,731 of SEQ ID NO: 1. Accordingly, the specification does not appear to teach that the primers hybridize to the end regions of the exons and thereby the specification does not appear to teach that the primers of SEQ ID NO: 82 and 84 amplify the complete region beginning at exon 18 and extending through the end of exon 23 or that the primers of SEQ ID NO: 83 and 84 amplify the complete region beginning at exon 19 and extending through the end of exon 23.

With respect to claims 77 and 79, the specification as originally filed does not appear to provide support for the concept of oligonucleotides consisting of 16 nucleotides of a region extending from the beginning of exon 19 through exon 20. In the response of June 2, 2006, it is stated that support for this embodiment may be found in Figure 1, which provides a schematic of the intron and exon regions. It is also stated that exon 19 through 20 corresponds to nucleotides 33,642 to 34,195 of SEQ ID NO: 1. However, Figure 1 does not clearly set forth the positions within exons 18, 19 and 23 to which the primers hybridize. Further, the specification does not teach that the region of exon 19 to 20 consists of nucleotides 33,642 to 34,195 and no evidence has been provided to support this conclusion. The response points to Figure 2C as providing support for "the sequence boundary between exon 19 and 20." However, while Figure 2C recites the terms "exon 19" and "exon 20," this figure does not disclose a fragment consisting of the complete region beginning with exon 19 and ending with exon 20 or subfragments thereof consisting of 16 or more nucleotides. The response

also points to Figure 6 of provisional application 60/260,080 as teaching a region extending from nucleotide 33,642 to nucleotide 34,195. However, while Figure 6 of the '080 application includes nucleotides 33,642 to 34,195, this figure does not specifically disclose a fragment consisting of nucleotides 33,642 to 34,195 or fragments thereof consisting of 16 or more nucleotides. As set forth in MPEP 2163.05, the disclosure of a genus does not necessarily provide basis for a subgenus within this genus. In the present situation, the disclosure of the genus of oligonucleotides of at least 16 nucleotides (page 13 of the specification) does not provide basis for the subgenus of oligonucleotides that consist of 16 or more nucleotides between the beginning of exon 19 and the terminus of exon 20.

5. Claims 50 and 76-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acids consisting of 16 or more **contiguous** nucleotides of SEQ ID NO: 1 or 2, does not reasonably provide enablement for nucleic acids consisting of 16 or more nucleotides selected from any sequences of SEQ ID NO: 1 or 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is noted that this rejection may be overcome by amendment of the claims to recite "consisting of 16 or more contiguous nucleotides" in place of "consisting of 16 or more nucleotides of SEQ ID NO:" and in place of "consisting of 16 or more nucleotides chosen from a region."

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Breadth of the Claims:

The claims are broadly drawn to nucleic acids consisting of 16 or more nucleotides of SEQ ID NO: 1 or 2 and nucleic acids consisting of 16 or more nucleotides chosen from a region extending from the beginning of exon 19 through exon 20 of SEQ ID NO: 1. The claims do not require that the 16 selected nucleotides are contiguous with one another. Accordingly, the claims include oligonucleotides which contain any 16 or more randomly arranged nucleotides from SEQ ID NO: 1 or 2 or from the exon19-20 region of SEQ ID NO: 1.

Nature of the Invention:

The claims are drawn to isolated nucleic acids comprising portions of the IKAP cDNA and genomic DNA. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F. 3d 1316, 1330 (Fed Cir. 2001).

State of the Art:

The specification teaches the complete cDNA sequence (SEQ ID NO: 2) and genomic sequence (SEQ ID NO: 1) of the IKAP gene. The IKBKAP genomic DNA spans 66,479 nucleotides. The specification further teaches two mutations in the IKBKAP gene: a) the "FD1" mutation located at bp6 within intron 20, wherein a thymine is replaced by a cytosine; and b) the "FD2" located at position 2396 (bp73 of exon 19) wherein a guanine is replaced by a cytosine, leading to a missense arginine to proline mutation at amino acid position 696. The specification and prior art do not teach any additional mutations in the IKBKAP gene and particularly does not teach any additional IKBKAP mutations associated with FD. Further, the specification and prior art do not teach any homologues or splice variants of the IKAP gene. There is no disclosure or support in the specification for additional nucleic acids consisting of any randomly selected 16 nucleotides of SEQ ID NO: 1 or 2.

The Predictability or Unpredictability of the Art and Degree of Experimentation:

The claims encompass nucleic acids which are not specifically defined in terms of their overall nucleic acid sequence or in terms of their functional activity. The prior art acknowledges the unpredictability in modifying the nucleotide sequence of a gene. Modification of even a single nucleotide within a coding or non-coding sequence can significantly alter the functional properties of that gene and protein encoded thereby. The specification does not provide any information as to regions of SEQ ID NO: 1 and 2 which are critical for functional activity and for maintaining the three dimensional structure of the encoded protein in order to

allow for the encoded protein to be associated with the occurrence of FD. There is no disclosure in the specification as to how nucleic acids which share only one nucleotide in common with the IKAP gene can be used to detect mutations in the IKAP gene or to detect deletions of exon 20. There is also no disclosure as to the degree of sequence identity shared between the IKAP gene and other genes which would allow one to modify the IKAP sequences and add flanking nucleotides of any length and identity, yet still maintain the properties of a nucleic acid as useful for detecting any mutation associated with FD. Thereby, it is highly unpredictable as to how modifying sequences within SEQ ID NO: 1 and 2 will effect the overall functional properties of the resulting gene. . It is unpredictable as to what would be the functional activity of a nucleic acid that consists of any 16 or more nucleotides chosen from any sequence within SEQ ID NO: 1 or 2 or exon 19-20, and arranged in any order. For instance, it is unpredictable as to how adding nucleotides of any identity or length to the terminus of fragments of 1 nucleotide of SEQ ID NO: 1 or 2. The addition of nucleotides of any identity to the terminus of these nucleic acids would be expected to significantly effect their functional activity. For instance, Accession No. ACD13384 discloses a nucleic acid comprising SEQ ID NO: 86 and additional flanking nucleotides wherein the nucleic acid has the activity of a p53 modifier. Similarly, Accession No. ACF67648 discloses an isolated nucleic acid comprising SEQ ID NO: 86, wherein the nucleic acid is from *Photorhabdus luminescens* and has antibacterial or antifungicidal activity. Thereby, the effect of adding nucleotides to the 3' or 5' end of fragments of the IKAP gene is highly unpredictable.

Extensive experimentation would be required to determine how to make and use oligonucleotides consisting of 16 or more random nucleotides of SEQ ID NO: 1 or 2, particularly because the claims do not set forth a specific functional activity for the oligonucleotides. With respect to the IKAP gene, it is unpredictable as to which residues within this gene of over 60Kb are important to the functional activity of the encoded protein and which nucleotides are variable in nature and are associated with the occurrence of FD. To identify additional genes or mutations requires extensive, trial-by-error experimentation in which researchers may be required to map genes, perform linkage analysis to determine the inheritance pattern of polymorphisms, sequence genes, identify specific mutations in the sequenced gene, analyze members of the population which have FD and individuals who do not have FD for the presence or absence of a polymorphism or mutation and try to ascertain which specific polymorphisms or mutations are associated with the occurrence of disease. Such experimentation is considered to be undue.

Amount of Direction or Guidance Provided by the Specification:

The specification does not provide any specific guidance as to how to predictably make and use nucleic acids consisting of 16 or more nucleotides chosen from any portion of SEQ ID NO: 1 or 2 and arranged in any order. While one could generate a significantly large genus of nucleic acids which contain any 16 or more nucleotides arranged in any order, and then assay each of these nucleic acids to try to determine their biological activity, such trial-by-error experimentation is considered to be undue. Providing methods for searching for

additional nucleic acids and trying to determine if the resulting nucleic acid will detect an undefined mutation associated with FD is not equivalent to teaching how to make and use specific nucleic acids.

Working Examples:

Again, the specification teaches only the IKAP genomic DNA of SEQ ID NO: 1, the IKAP cDNA of SEQ ID NO: 2, the probes of SEQ ID NO: 85 and 86 and a nucleic acid spanning the exon 19/21 junction (SEQ ID NO: 89). The specification teaches the use of contiguous fragments of SEQ ID NO: 1 or 2 as probes and as primers. However, the specification does not provide any working examples of how to predictably make and use nucleic acids consisting of any 16 randomly chosen nucleotides of SEQ ID NO: 1 or 2 arranged in any order.

Conclusions:

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate

enablement". In the instant case, the claims do not bear a reasonable correlation to the scope of enablement because the specification teaches only the full length cDNA and genomic DNA of the IKAP gene (i.e., SEQ ID NO: 2 and 1) and oligonucleotides consisting of contiguous nucleotides of SEQ ID NO: 1 and 2, whereas the claims encompass a significantly large genus of nucleic acids, in which the overall structural and functional properties of the nucleic acids are not clearly defined. As set forth above, in view of the unpredictability in the art, extensive experimentation would be required to make and use additional nucleic acids consisting of any randomly chosen nucleotides of SEQ ID NO: 1 or 2 arranged in any order because the does not teach a predictable means for determining which of the resulting nucleic acids will have the functional property of being capable of detecting a mutation associated with FD or a predictable means for determining other functional activities of the resulting nucleic acids. Additionally, the claims do not bear a reasonable correlation to the scope of enablement because the specification teaches only 2 specific members of the broadly claimed genus of oligonucleotides which detect any mutation in any gene associated with FD and oligonucleotides which consist of fragments thereto, but does not teach a representative number of other oligonucleotides containing any randomly chosen and arranged nucleotides of SEQ ID NO: 1 or 2. Accordingly, although the level of skill in the art of molecular biology is high, given the lack of disclosure in the specification and in the prior art, it would require undue experimentation for one of skill in the art to make and use the broadly claimed invention.

6. Claims 50 and 76-80 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

It is noted that this rejection may be overcome by amendment of the claims to recite "consisting of 16 or more contiguous nucleotides" in place of "consisting of 16 or more nucleotides of SEQ ID NO:" and in place of "consisting of 16 or more nucleotides chosen from a region."

The claims are broadly drawn to nucleic acids consisting of 16 or more nucleotides of SEQ ID NO: 1 or 2 and nucleic acids consisting of 16 or more nucleotides chosen from a region extending from the beginning of exon 19 through exon 20 of SEQ ID NO: 1. The claims do not require that the 16 selected nucleotides are contiguous with one another. Accordingly, the claims include oligonucleotides which contain any 16 or more randomly arranged nucleotides from SEQ ID NO: 1 or 2 or from the exon 19-20 region of SEQ ID NO: 1. The claims do not define the oligonucleotides in terms of a specific overall structure or function.

Nucleic acids which consist of 16 or more contiguous nucleotides of SEQ ID NO: 1 or 2 and nucleic acids consisting of SEQ ID NO: 82-85 meet the written description requirements. However, the specification does not provide an adequate written description of the claimed genus of nucleic acids that consist of

any 16 or more randomly selected and arranged nucleotides of SEQ ID NO: 1 or 2.

The specification teaches 2 mutations in the IKBKAP gene: a) the "FD1" mutation located at bp6 within intron 20, wherein a thymine is replaced by a cytosine; and b) the "FD2" located at position 2396 (bp73 of exon 19) wherein a guanine is replaced by a cytosine, leading to a missense arginine to proline mutation at amino acid position 696. The specification further teaches the complete cDNA sequence (SEQ ID NO: 2) and genomic sequence (SEQ ID NO: 1) of the IKBKAP gene. The IKBKAP genomic DNA spans 66,479 nucleotides.

The claims do not clearly define the nucleic acids in terms of their overall structure. A wide variety of nucleic acids comprise the nucleotide at position 34,201 or 33,714 of SEQ ID NO: 1 and 2, wherein such nucleic acids have significantly different functional activities from the nucleic acids of SEQ ID NO: 1 and 2. For instance, Accession No. ACD13384 discloses a nucleic acid comprising SEQ ID NO: 86 and additional flanking nucleotides wherein the nucleic acid has the activity of a p53 modifier. Similarly, Accession No. ACF67648 discloses an isolated nucleic acid comprising SEQ ID NO: 86, wherein the nucleic acid is from *Photorhabdus luminescens* and has antibacterial or antifungicidal activity. Accordingly, the claims are inclusive of nucleic acid molecules which have distinct biological activities from the disclosed nucleic acids of SEQ ID NO: 1 and 2.

Additionally, the claims do not set forth the specific order or identity of the nucleotides flanking the nucleotide at position 34,201 or 33,714 of SEQ ID NO: 1

and 2.Accordingly, the claims encompass nucleic acids which consist of the recited cytosine or guanine but which share any overall level of sequence identity with SEQ ID NO: 1 and 2 (e.g., 80%, 60%, 10% etc). The claims thereby encompass naturally and non-naturally variants of the FD gene, wherein the variants may include nucleotide substitutions, additions, deletions, translocations and truncations and splice variants and nucleic acids having distinct biological activities as compared to the FD gene.

The general knowledge in the art concerning homologues, mutants, allelic and splice variants does not provide any indication of how modification of the sequence of SEQ ID NO: 1 and 2 will effect the functional properties of SEQ ID NO: 1 and 2. The structure and function of one molecule does not provide guidance as to the structure and function of other molecules. Therefore, the description of the genomic sequence of SEQ ID NO: 1 and the cDNA sequence of SEQ ID NO: 2 is not representative of a genus of homologues, splice, mutant and allelic variants of SEQ ID NO: 1 and 2 and of other nucleic acids having unspecified functional activities different from that of SEQ ID NO: 1 and 2. A general statement in the specification of a desire to obtain gene sequences, homologues from other species, mutated species, and polymorphic sequences is not equivalent to providing a clear and complete description of specific sequences which fall within the claimed genus of nucleic acids.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for

purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". The limited information provided in the specification is not deemed sufficient to reasonably convey to one of skill in the art that Applicants were in possession of the claimed homologues, mutants, allelic and splice variants of SEQ ID NO: 1 and 2 or of a representative number of other oligonucleotides consisting of any randomly chosen and arranged 16 or more nucleotides of SEQ ID NO: 1 or 2. Therefore, the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 77 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Cohen (U.S. Patent No. 5,891,719; see attached alignment).

Cohen teaches an isolated nucleic acid encoding for IKBKAP (referred to therein as 'IKAP; see SEQ ID NO: 1 therein). The full length nucleic acid of Cohen shares 99% identity with present SEQ ID NO: 2 and differs from SEQ ID NO: 2 at 5 nucleotide positions over the disclosed 3999 nucleotides. The nucleic acid of Cohen contains a guanine at nucleotide position 2087, which corresponds to position 2397 of present SEQ ID NO: 2 and to position 33,714 of SEQ ID NO: 1.

In particular, with respect to claims 77 and 78, Cohen teaches a nucleic acid encoding amino acids 683-687 of SEQ ID NO: 2 therein (see claim 10 and col. 4-5). This nucleic acid of Cohen consists of nucleotides 2047-2091 of SEQ ID NO: 1 therein and is 100% identical to a fragment of present SEQ ID NO: 2 containing nucleotide 2397 and to a fragment of present SEQ ID NO: 1 containing nucleotide position 33,714. Thereby, the nucleic acid of Cohen which consists of a nucleotide sequence encoding amino acids 583-687 anticipates the claimed nucleic acids consisting of 16 or more nucleotides of SEQ ID NO: 2 and including nucleotide position 2397 and the claimed nucleic acids consisting of 16

or more nucleotides of exon 19-20 of SEQ ID NO: 1 and including nucleotide position 33,714.

8. Claims 77, 78, 79 and 80 are rejected under 35 U.S.C. 102(a) as being anticipated by Rubin (2002/0168656; cited in the IDS).

Rubin (page 1, column 2) discloses a cDNA encoding IKAP having GenBank Accession No. NM_003640. Rubin further teaches two mutations in the IKBKAP gene wherein the first mutation is a G to C transversion at nucleotide 2390 in exon 19 of Accession No. NM_003640 (i.e., position 2397 of SEQ ID NO: 2 and position 33714 of present SEQ ID NO: 1) and the second mutation is a T to C transition in position 6 of the donor splice site for exon 6 (page 1, column 2). Thereby, the nucleic acid of Rubin contains a C at the position corresponding to nucleotide position 2,397 of present SEQ ID NO: 2 and a C at the position corresponding to position 33,714 of present SEQ ID NO: 1. Rubin also teaches a fragment of exon 19 of the IKAP gene of 238 bp containing the FD2 major and minor alleles (i.e., the G and C alleles; col. 1, page 2). According, the nucleic acid of Rubin consists of 16 or more nucleotides of SEQ ID NO: 2 and includes nucleotide position 2397 and consists of 16 or more nucleotides of exon 19-20 of SEQ ID NO: 1 and includes nucleotide position 33,714 of present SEQ ID NO: 1.

9. Claims 77, 78, 79 and 80 are rejected under 35 U.S.C. 102(a) as being anticipated by Anderson (American Journal of Human Genetics (March 2001) 68: 753-758; cited in the IDS).

Anderson (page 754) discloses a cDNA encoding human IKBKAP having GenBank Accession No. NM_003640. Anderson further teaches two mutations in

the IKBKAP gene wherein the first mutation is a G to C transversion at nucleotide 2390 in exon 19 of Accession No. NM_003640 (i.e., position 2397 of SEQ ID NO: 2 and position 33714 of present SEQ ID NO: 1) and the second mutation is a T to C transition in position 6 of the donor splice site for exon 6 (page 754). Thereby, the nucleic acid of Anderson contains a C at the position corresponding to nucleotide position 2,397 of present SEQ ID NO: 2 and a C at the position corresponding to nucleotide position 33,714 of present SEQ ID NO: 1. Anderson also teaches a fragment of exon 19 of the IKAP gene of 238 bp containing the FD2 major and minor alleles (see, e.g., Figure 4). According, the nucleic acid of Anderson consists of 16 or more nucleotides of present SEQ ID NO: 2 and includes nucleotide position 2397 and consists of 16 or more nucleotides of exon 19-20 of present SEQ ID NO: 1 and includes nucleotide position 33,714.

10. Claims 77-79 are rejected under 35 U.S.C. 102(a) as being anticipated by Slaugenhaupt (American Journal of Human Genetics (March 2001) 68: 598-605; cited in the IDS).

Slaugenhaupt (page 600) discloses a 5.9 Kb cDNA encoding human IKBKAP having GenBank Accession No. AF153419. This cDNA is identical to the cDNA of present SEQ ID NO: 2 (i.e., Figure 7). Slaugenhaupt further teaches two mutations in the IKBKAP gene wherein the first mutation is a G to C transversion at nucleotide 2397 in exon 19, resulting in a arginine to proline missense mutation at amino acid position 696 and the second mutation is a T to C transition in position 6 of the donor splice site for exon 6 (page 602). The reference also teaches amplification products containing the 2 mutations wherein

the amplification products are generated by amplifying IKBKAP sequences using primers to exons 19 and 20/21 (page 599). The primer 19F disclosed by Slaugenhaupt consists of 19 nucleotides of SEQ ID NO: 1 and includes a G corresponding to nucleotide position 33,714 of present SEQ ID NO: 1 (see page 599). Accordingly, Slaugenhaupt teaches oligonucleotides consisting of 16 or more nucleotides of present SEQ ID NO: 2 and which include nucleotide position 2397 and oligonucleotides consisting of 16 or more nucleotides of exon 19-20 of present SEQ ID NO: 1 and which include nucleotide position 33,714.

11. Claim 78 is rejected under 35 U.S.C. 102(b) as being anticipated by Gill et al (GenBank Accession No. AF153419, published 02 January 2001).

Gill discloses a 5.9 Kb cDNA encoding human IKBKAP having GenBank Accession No. AF153419. This cDNA is identical to the cDNA of present SEQ ID NO: 2 (i.e., Figure 7). The cDNA of Gill includes a G at nucleotide position 2397 of present SEQ ID NO: 2. In the comments section, Gill teaches that this position contains a polymorphism, but Gill does not teach a C at position 2397.

12. Claim 78 is rejected under 35 U.S.C. 102(a) as being anticipated by Slaugenhaupt et al (GenBank Accession No. AF153419, published 28 February 2001; cited in the IDS).

Slaugenhaupt discloses a 5.9 Kb cDNA encoding human IKBKAP having GenBank Accession No. AF153419. This cDNA is identical to the cDNA of present SEQ ID NO: 2 (i.e., Figure 7). The cDNA of Slaugenhaupt includes a G at nucleotide position 2397. In the comments section, Slaugenhaupt teaches that

this position contains a polymorphism, but Slaugenhaupt does not teach a C at position 2397.

13. Claims 50 and 76-80 are rejected under 35 U.S.C. 102(a) as being anticipated by Boehringer Mannheim (Biochemicals for Molecular Biology. 1995. page 136).

The claims encompass oligonucleotides consisting of any 16 nucleotides of SEQ ID NO: 1 or 2 or a fragment of SEQ ID NO: 1 extending from exon 19 to exon 20, wherein the nucleotides may be arranged in any order, and wherein the oligonucleotides comprise a cytosine or guanine (i.e., nucleotide position 2,397 of SEQ ID NO: 2 or nucleotide position 33,714 of SEQ ID NO: 1) or wherein the oligonucleotide comprises a thymine or cytosine (nucleotide position 34,201 of SEQ ID NO: 1).

Boehringer Mannheim discloses oligonucleotides of 16 and 17 nucleotides, wherein the oligonucleotides include a G and a C (i.e., nucleotide position 2,397 of SEQ ID NO: 2 or nucleotide position 33,714 of SEQ ID NO: 1) and a T and a C (nucleotide position 34,201 of SEQ ID NO: 1). The oligonucleotides also contain additional A, G, C and T nucleotides and thereby consist of at least 16 nucleotides from SEQ ID NO: 1 and 2.

It is noted that this rejection may be overcome by amendment of the claims to recite "consisting of 16 or more contiguous nucleotides" in place of "consisting of 16 or more nucleotides of SEQ ID NO:" and in place of "consisting of 16 or more nucleotides chosen from a region."

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 65-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slaugenhaupt (American Journal of Human Genetics (March 2001) 68: 598-605; cited in the IDS) in view of Fodor (U.S. Patent NO. 5,968,740).

Slaugenhaupt (page 600) discloses a 5.9 Kb cDNA encoding human IKBKAP having GenBank Accession No. AF153419. This cDNA is identical to the cDNA of present SEQ ID NO: 2 (i.e., Figure 7). Slaugenhaupt teaches amplifying IKBKAP nucleic acids using primers 18F, 19F and 23R, which are identical to present SEQ ID NO: 82-84. Slaugenhaupt does not teach packaging the IKBKAP primers in a kit.

However, reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. In particular, the Fodor (column 3) discloses the general concept of kits for performing nucleic acid hybridization methods and discloses that kits may include any of the reagents necessary for performing methods for detecting a target nucleic acid. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the IKBKAP primers in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)-272-0735.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

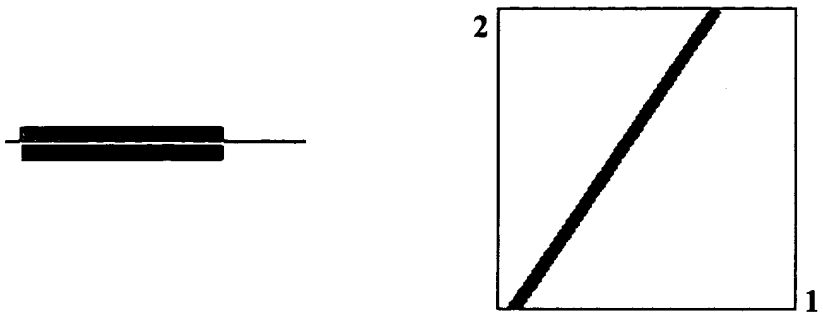
Carla Myers
Art Unit 1634

CARLA J. MYERS
PRIMARY EXAMINER

Alignment of SEQ ID NO. 2 and Cover

Sequence 1: lcl|seq_1
Length = 5924 (1 .. 5924)

Sequence 2: gi|7221053|gb|AR070165.1|AR070165Sequence 1 from patent US 5891719
Length = 3999 (1 .. 3999)



NOTE:Bitscore and expect value are calculated based on the size of the nr database.

NOTE:If protein translation is reversed, please repeat the search with reverse strand of the query sequence.

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 Score = 7660 bits (3984),  Expect = 0.0
 Identities = 3994/3999 (99%), Gaps = 0/3999 (0%)
 Strand=Plus/Plus

Query  311   ATGCGAAATCTGAAATTATTTCGGACCCTGGAGTTCAGGGATATTCAAGGTCCAGGGAAT  370
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  1     ATGCGAAATCTGAAATTATTTCGGACCCTGGAGTTCAGGGATATTCAAGGTCCAGGGAAT  60

Query  371   CCTCAGTGCTTCTCTCTCCGAACTGAACAGGGGACGGTGCTCATTGGTTCAGAACATGGC  430
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Sbjct  61    CCTCAGTGCTTCTCTCTCCGAACTGAACAGGGGACGGTGCTCATTGGTTCAGAACATGGC  120

Query  431   CTGATAGAAGTAGACCCTGTCTCAAGAGAAGTGAAAAATGAAGTTTCTTTGGTGGCAGAA  490
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Sbjct  181   GGCTTTCTTCCAGAGGATGGAAGTGGCCGCATTGTTGGTGTTCAGGACTTGCTGGATCAG  240

Query  551   GAGTCTGTGTGTGTGGCCACAGCCTCTGGAGACGTCATACTCTGCAGTCTCAGCACACAA  610
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Sbjct  241   GAGTCTGTGTGTGTGGCCACAGCCTCTGGAGACGTCATACTCTGCAGTCTCAGCACACAA  300

Query  611   CAGCTGGAGTGTGTTGGGAGTGTAGCCAGTGGTATCTCTGTTATGAGTTGGAGTCCTGAC  670
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Sbjct  301   CAGCTGGAGTGTGTTGGGAGTGTAGCCAGTGGTATCTCTGTTATGAGTTGGAGTCCTGAC  360

Query  671   CAAGAGCTGGTGCTTCTTGCCACAGGTCAACAGACCCTGATTATGATGACAAAAGATTTT  730
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Query  731   GAGCCAATCCTGGAGCAGCAGATCCATCAGGATGATTTTGGTGAAAGCAAGTTTATCACT  790
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Sbjct  481   GTTGGATGGGGTAGGAAGGAGACACAGTTCCATGGATCAGAAGGCAGACAAGCAGCTTTT  540

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Sbjct  601   CGGGGGGATGGACAGTTTTTTGCTGTGAGTGTTGTTTGCCCAGAAACAGGGGCTCGGAAG  660

Query  971   GTCAGAGTGTGGAACCGAGAGTTTGCTTTGCAGTCAACCAGTGAGCCTGTGGCAGGACTG  1030
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Sbjct  661   GTCAGAGTGTGGAACCGAGAGTTTGCTTTGCAGTCAACCAGTGAGCCTGTGGCAGGACTG  720

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Sbjct  841   CCCTTCCTTAAAGATGAGGTTAAGGTAAATGACTTGCTCTGGAATGCAGATTCCTCTGTG  900

Query  1211  CTTGCAGTCTGGCTGGAAGACCTTCAGAGAGAAGAAAGCTCCATTCCGAAAACCTGTGTT  1270
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Query  1631  GTTCTAGATGCCAGTAACCAGATTTCTGTTTATAAATGTGGTGATTGTCCAAGTGCTGAC  1690
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Query  3011  GATTTGGTCCTCATGGTAGCTGAGAAGTCACAGAAGGATCCCAAAGAATATCTTCCATTT  3070
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Query  3071  CTTAATACACTTAAGAAAATGGAAACTAATTATCAGCGGTTTACTATAGACAAATACTTG  3130
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Query  3131  AAACGATATGAAAAAGCCATTGGCCACCTCAGCAAATGTGGACCTGAGTACTTCCCAGAA  3190
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Query  3191  TGCTTAAACTTGATAAAAGATAAAAACTTGTATAACGAAGCTCTGAAGTTATATTCACCA  3250
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Sbjct  2881  TGCTTAAACTTGATAAAAGATAAAAACTTGTATAACGAAGCTCTGAAGTTATATTCACCA  2940

Query  3251  AGCTCACAACAGTACCAGGATATCAGCATTGCTTATGGGGAGCACCTGATGCAGGAGCAC  3310
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  2941  AGCTCACAACAGTACCAGGATATCAGCATTGCTTATGGGGAGCACCTGATGCAGGAGCAC  3000

Query  3311  ATGTATGAGCCAGCGGGGCTCATGTTTGCCCGTTGCGGTGCCCACGAGAAAGCTCTCTCA  3370
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3001  ATGTATGAGCCAGCGGGGCTCATGTTTGCCCGTTGCGGTGCCCACGAGAAAGCTCTCTCA  3060

Query  3371  GCCTTTCTCACATGTGGCAACTGGAAGCAAGCCCTCTGTGTGGCAGCCCAGCTTAACTTT  3430
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3061  GCCTTTCTCACATGTGGCAACTGGAAGCAAGCCCTCTGTGTGGCAGCCCAGCTTAACTTT  3120
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Query  3431  ACCAAAGACCAGCTGGTGGGCCTCGGCAGAACTCTGGCAGGAAAGCTGGTTGAGCAGAGG  3490
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3121  ACCAAAGACCAGCTGGTGGGCCTCGGCAGAACTCTGGCAGGAAAGCTGGTTGAGCAGAGG  3180

Query  3491  AAGCACATTGATGCGGCCATGGTTTTGGAAGAGAGTGCCCAGGATTATGAAGAAGCTGTG  3550
             |||||||||||||||||||||||||||||||| ||||||||||||||||||||||||||
Sbjct  3181  AAGCACATTGATGCGGCCATGGTTTTGGAAGAGTGTGCCCAGGATTATGAAGAAGCTGTG  3240

Query  3551  CTCTTGCTGTTAGAAGGAGCTGCCTGGGAAGAAGCTTTGAGGCTGGTATACAAATATAAC  3610
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3241  CTCTTGCTGTTAGAAGGAGCTGCCTGGGAAGAAGCTTTGAGGCTGGTATACAAATATAAC  3300

Query  3611  AGACTGGATATTATAGAAACCAACGTAAAGCCTTCCATTTTAGAAGCCCAGAAAAATTAT  3670
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3301  AGACTGGATATTATAGAAACCAACGTAAAGCCTTCCATTTTAGAAGCCCAGAAAAATTAT  3360

Query  3671  ATGGCATTTCTGGACTCTCAGACAGCCACATTCAGTCGCCACAAGAAACGTTTATTGGTA  3730
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3361  ATGGCATTTCTGGACTCTCAGACAGCCACATTCAGTCGCCACAAGAAACGTTTATTGGTA  3420

Query  3731  GTTCGAGAGCTCAAGGAGCAAGCCCAGCAGGCAGGTCTGGATGATGAGGTACCCCACGGG  3790
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3421  GTTCGAGAGCTCAAGGAGCAAGCCCAGCAGGCAGGTCTGGATGATGAGGTACCCCACGGG  3480

Query  3791  CAAGAGTCAGACCTCTTCTCTGAAACTAGCAGTGTCGTGAGTGGCAGTGAGATGAGTGGC  3850
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3481  CAAGAGTCAGACCTCTTCTCTGAAACTAGCAGTGTCGTGAGTGGCAGTGAGATGAGTGGC  3540

Query  3851  AAATACTCCCATAGTAACTCCAGGATATCAGCGAGATCATCCAAGAATCGCCGAAAAGCG  3910
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3541  AAATACTCCCATAGTAACTCCAGGATATCAGCGAGATCATCCAAGAATCGCCGAAAAGCG  3600

Query  3911  GAGCGGAAGAAGCACAGCCTCAAAGAAGGCAGTCCGCTGGAGGACCTGGCCCTCCTGGAG  3970
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3601  GAGCGGAAGAAGCACAGCCTCAAAGAAGGCAGTCCGCTGGAGGACCTGGCCCTCCTGGAG  3660

Query  3971  GCACTGAGTGAAGTGGTGCAGAACACTGAAAACCTGAAAGATGAAGTATACCATATTTTA  4030
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3661  GCACTGAGTGAAGTGGTGCAGAACACTGAAAACCTGAAAGATGAAGTATACCATATTTTA  3720

Query  4031  AAGGTACTCTTTCTCTTTGAGTTTGATGAACAAGGAAGGGAATTACAGAAGGCCTTTGAA  4090
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3721  AAGGTACTCTTTCTCTTTGAGTTTGATGAACAAGGAAGGGAATTACAGAAGGCCTTTGAA  3780

Query  4091  GATACGCTGCAGTTGATGGAAAGGTCACTTCCAGAAATTTGGACTCTTACTTACCAGCAG  4150
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3781  GATACGCTGCAGTTGATGGAAAGGTCACTTCCAGAAATTTGGACTCTTACTTACCAGCAG  3840

Query  4151  AATTCAGCTACCCCGGTTCTAGGTCCCAATTCTACTGCAAATAGTATCATGGCATCTTAT  4210
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3841  AATTCAGCTACCCCGGTTCTAGGTCCCAATTCTACTGCAAATAGTATCATGGCATCTTAT  3900

Query  4211  CAGCAACAGAAGACTTCGGTTCCTGTTCTTGATGCTGAGCTTTTTATACCACCAAAGATC  4270
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  3901  CAGCAACAGAAGACTTCGGTTCCTGTTCTTGATGCTGAGCTTTTTATACCACCAAAGATC  3960

Query  4271  AACAGAAGAACCCAGTGGAAGCTGAGCCTGCTAGACTGA  4309
             |||||||||||||||||||||||||||||||||||||||
Sbjct  3961  AACAGAAGAACCCAGTGGAAGCTGAGCCTGCTAGACTGA  3999
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